Weitz-Scheffer Type Asymmetric Epoxidation by Utilization of Molecular Oxygen under Phase Transfer Condition

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COMMUNICATION

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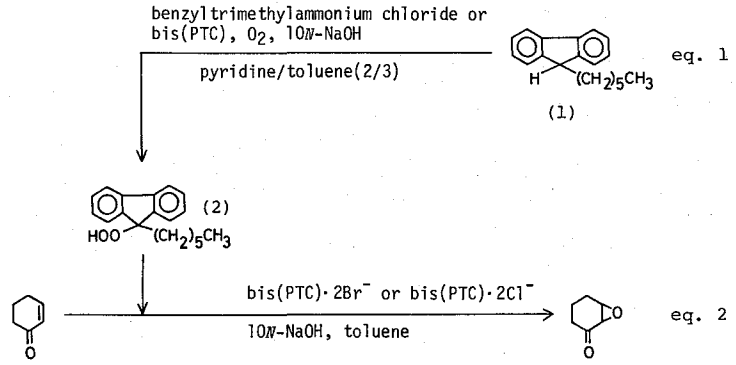
Epoxidation is an important process for chemical transformation of organic compounds. Major routes to synthesize epoxides have been based on one-oxygen atom transfer from hydroperoxides and peracids to alkenes sometimes catalyzed by transition metal complexes. A problem to be solved is that the process necessarily involves handling of hazardous peroxide which may be even more dangerous particularly in large scale reaction. From this view, direct utilization of stable molecular oxygen for epoxidation via *in situ* formation of hydroperoxide to oxo-metal complexes has been studied and a number of results have been published.[1] However, for preparation of optically active epoxides by this way, the examples are rare.[2] As mentioned in our previous report,[3] 9-hexyl-9-hydroperoxyfluorene (2) was found to be much better oxidizing agent than simple alkyl hydroperoxides for improving stereoselectivity of Weitz-Scheffer type asymmetric epoxidation (eq. 2).

Sprinzak reported a preparation of 9-hexyl-9-hydroperoxyfluorene (2) from (1) and dry oxygen gas catalyzed by Triton B at −10°C in dry pyridine.[4] Recently, however, we found much easier preparation of the hydroperoxide by use of benzyltrimethylammonium chloride under phase transfer condition (eq. 1).[5] This finding (eq. 1) in addition to our previous work (eq. 2) suggested that the hydroperoxide formation and asymetric epoxidation therewith could



Scheme 1

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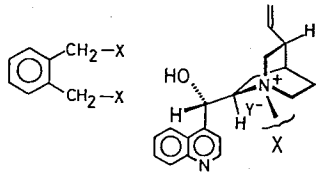

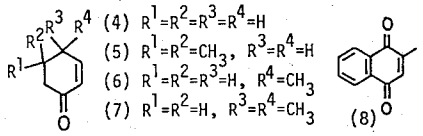

Scheme 2

be performed successibly in a one-pot in the presence of the same chiral phase transfer catalyst. Thus, as a typical experiment, oxygen gas was introduced into a solution of 9-hexylfluorene (1) (1.5 mmol), 10*N*–NaOH (36 μl), bis (PTC) from (+)-cinchonine (3a or 3b, 0.01 mmol) for 24 hr at room temp. To this solution was added cyclohexenone (1 mmol) and the same PTC (0.01 mmol) as well as 10*N*–NaOH (10 μl) to ensure satisfactory chemical conversion. The mixture was again stirred at -10°C for 1~3 days. After the period, the reaction mixture was washed with water to remove the catalyst and NaOH, and a fraction containing the epoxyketone was separated simply from fluorenol by distillation (20 mm) which was isolated pure by use of preparative VPC (5% XE–60, 3 m, 160°C). The optical yields were calculated from their optical rotation.[3)]

Thus, the hydroperoxidation and epoxidation proceeded smoothly in one-pot, and as shown in the Table the epoxyketones were obtained with the chemical yield ranging over 60–85% in addition to a few exceptions.

With regard to the enantioselectivity, cyclohexenone (4) gave 44% e.e. (run 1) and 54% e.e. (run 6) in the presence of bis (PTC), (3a) and (3b), respectively. These values appeared

Table I. Asymmetric Epoxidation of Cyclohexenones Catalyzed by (3a) and (3b) After Hydroperoxide Formation

run	bis (PTC)	substrate	react. temp.	% chem. yield	$[\alpha]_{578}$/°*	% e.e.	configuration
1	(3a)	4	−20°C	34	−85.1	44	2*S*, 3*S*
2	(3a)	5	−20	57	+5.1	9	—
3	(3a)	6	r.t.	82	−24.8	—	—
4	(3a)	7	r.t.	51	−17.1	—	—
5	(3a)	8	−20	76	+5.1	4	2*S*, 3*R*
6	(3b)	4	−20	85	−104.6	54	2*S*, 3*S*
7	(3b)	5	−20	80	+4.0	7	—
8	(3b)	6	r.t.	68	−29.4	—	—
9	(3b)	7	r.t.	13	−19.9	—	—
10	(3b)	8	−20	82	−1.5	1	2*S*, 3*R*

*) Optical rotation at ambient temperature in methylene chloride

to be 10~20% lower than those obtained from the same epoxidation by use of the isolated and purified fluorenyl hydroperoxide under the same conditions.[3] Although the chloride (3b) showed considerably higher catalytic activity than the bromide (3a), the enantioselectivities therefrom were found to be similar (44 and 54%). Epoxidation of the substrate (5) showed only 9% e.e. (run 2) and 7% e.e. (run 7) with (3a) and (3b) respectively. The same is the cases with substrate (8) (run 5 and 10). This feature is similar to those reported by Wynberg,[6] and the reason for the low selectivity remains unknown. The substrates (6) and (7) afforded the epoxyketones having optical rotations given in the Table whose optical purity are unknown and an attempt to determine e.e.s by use of NMR with chiral shift reagent were unsuccessful.

Although, the observed stereoselectivities were unsatisfactory, the present study is the first to obtain optically active epoxyketones in one-pot by use of molecular oxygen as such without any isolation process of the hazardous hydroperoxide.

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